REMARKS

Claims 1-24, 26-36, 38-55 are currently pending in this application after entry of the instant response. Claims 25 and 37 are cancelled. Claim 47 is withdrawn from consideration. Claims 1-24, 26-36, 38-46 and 48-55 are rejected.

Applicants acknowledge that claims 48, 49, 51, 52 and 53 have been found free of the art.

Claims 38 and 39 have been amended to depend from pending claim 20 in view of the cancellation of claim 37.

Claims 4, 21-22, 36, and 42 have been amended to correct spelling and grammatical errors. No new matter has been introduced by these amendments.

Applicants reserve the right to file a continuing application directed to the withdrawn and/or cancelled claims which continuing application is entitled to priority of the present invention.

Reconsideration and withdrawal of the pending rejections is respectfully requested in view of the amendments and remarks submitted herein.

Response to Rejections under 35 U.S.C. §112

Claims 38-39 have been rejected under 35 U.S.C. §112, second paragraph for being unclear and indefinite because they are dependent on cancelled claim 37. Applicants have cancelled claim 38 rendering this rejection moot. Claims 38 and 39 have been amended to depend from claim 20. Reconsideration and withdrawal of these §112 rejections to claims 38 and 39 are respectfully requested in view of the amendments to the claims.

Claim 38 has been rejected under 35 U.S.C. §112, second paragraph for the recitation "blocker probes" rather than "blocker probe" thereby lacking support in claim 20 or 37 from which the instant claim depends. Claim 38 has been amended to place the claim in a singular format for the recitations "blocker probes" and "capture sequence probes." Reconsideration and withdrawal of these §112 rejections to claim 38 is respectfully requested in view of the amendments to the claim.

Response to Rejections under 35 U.S.C. §102

Claims 1-5, 7-24, 26, 28-36, 38-44, and 46 are rejected under 35 U.S.C. §102(b) as being anticipated by Collins, et al. (USPN: 5,750,338). Applicants respectfully disagree with the Examiner's contention.

Collins does not anticipate claims 1-21, 38, 39 and 50-55 in view of "blocker probes" because contrary to the Examiner's contention, the background support of Collins is not equivalent to the claimed blocker probes.

These claims recite methods using a capture sequence probe (capture probe), a signal sequence probe (signal probe), and a blocker probe. The capture probe and signal probe bind to a target sequence, while the blocker probe binds to excess, non-hybridized capture probe. There are three types of probes, *i.e.*, capture probe, signal probe, and blocker probe. Applicants respectfully direct the Examiner's attention to Figure 2 of the instant invention for an illustration of the use of blocker probes in view of the capture probe and signal probe.

In contrast, the Collins publication at Column 7, lines 14-48 and Figure 3 (as cited by the Examiner) describes a first probe and a labeled second probe, a background support, and a target capture support. The first and second probes bind to a target, and the background support

binds to the unbound labeled second probe, while the target capture support binds to the first probe, which is used to capture the target. The Examiner has characterized the first probe as being equivalent to the claimed capture probe, and the second probe as being equivalent to the claimed signal probe. Applicants respectfully disagree with the Examiner's characterization of Collins for the following reasons.

The first probe described in Collins contains a binding ligand and is complementary to a part of the target sequence. In Collins' assay, the first probe functions to separate the target from the sample mixture by means of an immobilized binding partner for the binding ligand on the first probe.

Meanwhile, the second probe described in Collins is detectably labeled and is also complementary to part of the target sequence. This probe is used in the Collins' assay to detect the target sequence complex. However, Collins is concerned that excess labeled probe will increase the background signal (see, Collins, Col. 6, lns. 26-27). To avoid this problem, Collins uses a "background support" and adds a second ligand to the second probe (col. 6, lns. 42-54), where the background support has an anti-ligand moiety capable of binding the second ligand.

The instant claims are distinguishable from the Collins assay. The instant claims are not concerned with capturing and separating excess, non-hybridized signal sequence, as is the Collins publication. Instead, the instant claims separate excess, non-hybridized CAPTURE probe.

In addition, the instant invention uses blocker probes and does not use a background support. These are not equivalent.

Applicants direct the Examiner's attention to Column 6, lines 54-57 of Collins, which defines "background support" to include filters and membranes as well as retrievable

supports, and that binding to the background support does not need to be releasable. The background support of Collins is not a probe at all, but is a support that binds to the second probe. Indeed, Collins does not teach or suggest the use of a nucleic acid probe to separate any other sequence; and Collins certainly does not teach or suggest use of a nucleic acid probe to separate a capture probe as is claimed.

Therefore, because Collins' background support is not a nucleic acid probe and does not function like the claimed blocker probes which bind to excess capture probe, Collins does not anticipate the claimed method of detecting a target nucleic acid using a capture probe, signal probe, and blocker probe, where the blocker probe hybridizes to excess non-hybridized capture probe. Reconsideration and withdrawal of the §102 rejection to claims 1-21, 38, 39, and 50-55 is respectfully requested.

In addition, Collins does not anticipate claims 1, 15-17, 22-24, 26-36, 40-46, and 48, which specifically require an unlabeled probe. The Examiner points to col. 22, lines 10-19 and col. 24, lines 42-48 of Collins for support of an unlabeled signal sequence probe. Contrary to the claimed invention, Collins requires at least one labeled probe for detection; whereas, the claimed invention does not. In fact, the Examiner has pointed to Example 1, column 24, lines 42-48 which simply describes experimental controls for binding. One control reaction has a tailed first probe and an unlabeled second probe, while the other control reaction has a tailed first probe and a labeled second probe. However, this section of Example 1 simply indicates experimental control reactions, and not what is the inventive method of Collins.

Similarly, the text at Col. 22, lines 10-19, describes another embodiment utilizing a first and a second probe as a control for their assay. The second probe has unlabeled dA

residues which are recognized by dT-magnetic beads. In this embodiment, the first probe of Collins is detectably labeled with ^{32}P to enable detection of the target. This first probe detects the target nucleic acid, and is therefore labeled and thereby detectable. Therefore, contrary to the Examiner's contention that these sections support an unlabeled signal probe, applicants assert that the unlabeled probe described in Collins is a control example and Collins relies on a detectable label even in this example. Furthermore, the Examiner appears to have misread the section which teaches a probe that has unlabeled dA residues because this is allegedly similar to the claimed unlabeled capture probe. Neither of the claimed probes is directly labeled; whereas, Collins' signal probe is directly labeled. For the above reasons, Collins does not describe an unlabeled signal probe. Reconsideration and withdrawal of the §102 rejections to claims 1, 22, and 40 are respectfully requested.

With respect to claims 22-24, 26-31, and 33-36 directed to use of an antibody for target detection, the Examiner contends that Collins teaches a method of using an antibody which recognizes the hybrid complex as supported at col. 24, lines 49-67 and col. 29, table 4, steps 7-8. However, this section of Collins uses magnetized beads having dT residues to bind to a probe having dA residues in order to separate the target probe complex. Steps 7-8 of Table 4 are directed to binding the probe-target complex to dT_{3000}-nitrocellulose and incubating the filter in blocking buffer. Neither of these sections describes the use of an antibody to bind the hybrid complex where the antibody is detectably labeled. Because Collins does not describe using an antibody that recognizes the hybrid complex formed between the target nucleic acid and signal probe, applicants assert that Collins does not anticipate the invention of claims 22-24, 26-31, and

33-36. Reconsideration and withdrawal of the rejection to claims 22-24, 26-31, and 33-36 are respectfully requested.

Since Collins does not teach or suggest the use of blocker probes for binding to non-hybridized capture probe, the use of unlabeled probes, or the use of an antibody for binding the target-signal probe hybrid complex, and because each and every element of a claim needs to be taught in order for a reference to be anticipatory, applicants assert that Collins does not anticipate the instant claims. Reconsideration and withdrawal of the §102 rejections to claims 1-5, 7-24, 26, 28-36, 38-44, and 46 are respectfully requested.

Response to Rejections under 35 U.S.C. §103

Claims 6, 27, 45, 50, 54-55 have been rejected under 35 U.S.C. §103(a) as being unpatentable over Collins, et al. (USPN: 5,750,338) in view of Shah, et al. (USPN: 5,629,156) for teaching a method of detecting a target nucleic acid where two biotins are attached to capture probes and also for teaching bridge probes comprising a polyA tail. Applicants respectfully disagree with the Examiner's contention.

With respect to claims 6, 27, and 45, the Examiner alleges that Collins in view of Shah renders these claims that are directed to biotin molecules attached to the capture sequence probe as obvious. The invention recited in these claims utilizes a capture sequence probe (capture probe), a signal sequence probe (signal probe), and a target nucleic acid, where the capture sequence probe is biotinylated at both ends of the probe for detecting a target nucleic acid.

As previously mentioned, Collins does not teach or suggest a method of using a blocker probe to bind excess non-hybridized capture probe. Collins does not teach or suggest the

use of an unlabeled signal probe. Collins does not teach or suggest use of an antibody which recognizes a target-signal probe hybrid complex. As a result, the Collins method does not teach or suggest the claimed method for detecting the target nucleic acid. Furthermore, the Office Action states that "Collins et al. did not specifically teach two biotins attached to capture probes...." (Office Action; page 8). Thus, the Collins method does not teach or provide guidance for the use of two different nucleic acid probes for detecting a target nucleic acid where one probe has two biotins attached.

The Examiner has further combined Shah with Collins to assert the method of hybridizing a target nucleic acid to a capture probe and a signal sequence probe, where the capture probe has two biotins attached, and detecting the bound hybrid as recited in claims 6, 27, and 45 is obvious. Applicants respectfully disagree with this rejection.

Regarding claims 50, 54, and 55 directed to bridge probes, the Office Action states that Collins in view of Shah teaches the "use of dA-tailed probes comprising repeat units (bridge probes) which bind to both target and dT derivitized supports to form a stable target capture complex (see column 8, lines 44-54)." Applicants respectfully disagree with this contention that it would have been obvious to the skilled artisan to modify the method of detecting a target nucleic acid as taught by Collins, et al. with the step of adding dA-tailed probes comprising repeat units of Shah to result in the claimed invention.

Shah does not remedy the insufficiencies of the Collins method to result in the claimed method of hybridizing a target nucleic acid to a capture probe and a signal sequence probe, where the excess capture probe is separated using a blocker probe, or where the signal probe is unlabeled, or where the antibody that recognizes hybrids binds the target-signal probe hybrid complex. If the limitations of the independent claims are not taught or suggested by

either reference, a prima facie case of obviousness has not been established. Applicants respectfully request reconsideration and withdrawal of this §103 rejection.

In summary, the Shah reference does not remedy the defects of Collins with respect to blocker probes, unlabeled probe, biotinylated capture probe at the 5' and 3' ends, bridge probes, and dA-tailed bridge probes. The method described by Collins or Shah, either alone or in combination, does not describe the claimed methods. Reconsideration and withdrawal of the §103 rejection to claims 6, 27, 45, 50, 54 and 55 are respectfully requested.

Double Patenting

Claims 1-24, 26-36, 38-46, 48-55 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-52 and 54-92 of copending Application No. 10/311,645 (Publn. No. US 2004/0214302). Since the conflicting claims have not in fact been patented, this is a provisional obviousness-type double patenting rejection.

In response, applicants respectfully request that the provisional double-patenting rejection be held in abeyance due to the provisional nature of the rejection until one of the applications is allowed. Upon notice of otherwise allowable subject matter, applicants will address the rejection. Applicants note that it is proper when dealing with otherwise allowable subject matter in co-pending applications to withdraw a provisional rejection in the most advanced application, allow it to issue, and make a (non-provisional) rejection in the remaining application.

Thus, applicants respectfully submit that the invention as recited in the claims as presented herein is allowable over the art of record, and respectfully request that the respective rejections and objections be withdrawn.

CONCLUSION

Based on the foregoing amendments and remarks, applicants respectfully request reconsideration and withdrawal of the rejection of claims and allowance of this application. Applicants respectfully believe that the subject application is patentably distinguished over the art and that the claims are in condition for allowance. An action passing this case to issue is courteously urged.

AUTHORIZATION

The Commissioner is hereby authorized to charge any additional fees which may be required for consideration of this Amendment to Deposit Account No. **13-4500**, Order No. 2629-4017. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

In the event that an extension of time is required, or which may be required in addition to that requested in a petition for an extension of time, the Commissioner is requested to grant a petition for that extension of time which is required to make this response timely and is hereby authorized to charge any fee for such an extension of time or credit any overpayment for an extension of time to Deposit Account No. **13-4500**, Order No. 2629-4017. A DUPLICATE OF THIS DOCUMENT IS ATTACHED.

Respectfully submitted,
MORGAN & FINNEGAN, L.L.P.

Dated: March 8, 2006

By: _____
Evelyn M. Kwon
Registration No. 54,246

Correspondence Address:
MORGAN & FINNEGAN, L.L.P.
3 World Financial Center
New York, NY 10281-2101

(212) 415-8700 Telephone
(212) 415-8701 Facsimile